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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,708	11/21/2003	Shigeru Ohno	245819US0	8844

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EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/717,708	OHNO ET AL.	
	Examiner	Art Unit	
	Louis D Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the Restriction was received on 10/25/2004. Claims 1-4 are pending in the instant application. Applicants elected the subject matter of group I, drawn to an agent containing RGD-CAP and a method of using RGD-CAP to suppress mineralization and adhesion in the periodontal ligament. Original claim 3 is withdrawn by the examiner from further consideration pursuant to 37 CFR 1.142(b). Claims 1,2 and 4 are currently under examination.

Election with Traverse

Applicant's election with traverse of group I in the reply filed on 10/25/2004 is acknowledged. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the grounds of restriction for reasons of record as discussed below.

Applicant argues that the examiner has not offered examples of a compound capable of inducing RGD-CAP over expression and that the operative material in the claims of both Group I and II is RGD-CAP and that the action to be accomplished is the same in both instances. As stated in the previous action the invention of Group I reads on an agent containing the protein of RGD-CAP, while the invention of group II merely over expresses RGD-CAP. There is no requirement in Group II of treating the cells with the protein RGD-CAP. Further, the term over expression is interpreted to mean that the transcription and translation of an RGD-CAP gene or cDNA is increased in the cells of Group II. This does not require the protein of Group I. The over expression of RGD-CAP in the cells of Group II could be accomplished by transfection with an RGD-CAP cDNA or treatment with a transcription factor known to induce RGD-CAP

expression from a native gene. There is no evidence presented that RGD-CAP can act like an autocrine molecule to increase its own rate of expression. The invention of group I requires the protein RGD-CAP, while the invention of group II does not. Neither invention requires the other.

Applicant further argues that the Patent and Trademark Office has not demonstrated a sufficient search burden between the inventions of Groups I and II. However, as stated above the invention of Group I reads on the protein RGD-CAP, while the invention of Group II reads on a cDNA encoding RGD-CAP. The protein and the cDNA encoding it have different status in the art and their searches are not co-extensive. Therefore the examiner has withdrawn claim 3 from examination, for being directed to patentably different subject matter than the elected invention. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 1 and 2 are drawn to an agent containing RGD-CAP. The claim does not require the agent to have any structural limitations. The claims are drawn to a genus of agents that are defined solely by the presence of RGD-CAP and the ability to suppress mineralization in the periodontal ligament and to prevent the adhesion of teeth.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/ or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is the requirement that the agent contain RGD-CAP. There is no identification or contemplation of any other component of the agent, nor the functional or structural characteristics of these components. Further, the specification fails to provide any description of the kinds agents that would suppress mineralization in the periodontal ligament and to prevent the adhesion of teeth. While the specification contemplates a general agent containing RGD-CAP, it does not specify the precise nature of the agent. The specification does not disclose any agent containing RGD-CAP, other than RGD-CAP alone, with the ability to suppress mineralization in the periodontal ligament and to prevent the adhesion of teeth. At the time the invention was filed, agents containing RGD-CAP were not known in the art of record to suppress mineralization in the periodontal ligament and to prevent the adhesion of teeth. The structural characteristics of any other of the agent's components are not contemplated in the specification. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristic, the specification does not provide adequate written description of the claimed genus.

The Revised Interim Guidelines state ' when there is substantial variation with the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Column 2, page 71436, or

the Revised Interim Guidelines for Written Description). Case law concurs, stating, "simply describing large genus of compounds is not sufficient to satisfy written description requirement as to particular species or sub-genus" *Fujikawa v. Wattanasin*, 39 USPQ2d 1895 (CA FC 1996). Furthermore, *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Thus, the specification does not meet the written description provision of 35 U.S.C. 112, first paragraph, for an agent containing RGD-CAP other than RGD-CAP alone. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

Claims 1,2 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable an RGD-CAP protein from any species. The specification does not provide guidance on how to make or use a non-human RGD-CAP protein. While the specification contemplates the use of non-human RGD-CAP protein to suppress mineralization in the periodontal ligament and to prevent the adhesion of teeth, no evidence is presented that these sequences are capable of doing so. The specification contemplates that the

invention can performed with any protein having 70% or greater homology with human RGD-CAP. However, the specification does not teach what functional or structural domains must be conserved between variants and full-length human RGD-CAP protein. The art of record at the time of filing does not teach that an agent containing variants of human RGD-CAP protein can suppress mineralization in the periodontal ligament and prevent the adhesion of teeth. Further, the functional or structural domains of full-length human RGD-CAP that suppress mineralization in the periodontal ligament and prevent adhesion of teeth are not taught in art or the specification. Finally, none of the working examples disclose the use of RGD-CAP from other species, or human variants thereof.

The specification does not enable any agent containing RGD-CAP. Specifically, the specification does not provide guidance on how to make an agent comprising full-length human RGD-CAP or variants thereof. The specification does not identify or contemplate any other component of the agent, nor the functional or structural characteristics of these components. Further, the specification fails to provide any description of the kinds of agents that would suppress mineralization in the periodontal ligament and prevent the adhesion of teeth. While the specification contemplates a general agent containing RGD-CAP, it does not specify the precise nature of the agent. The specification discloses how to make full-length human RGD-CAP by using a plasmid encoded full-length human RGD-CAP in a bacterial expression system. However, the working examples does not teach how to make any agent containing non-human RGD-CAP or variants of full-length human RGD-CAP, except for an agent containing only human full-length RGD-CAP. At the time the invention was filed, agents containing full-length

or variants of human RGD-CAP were not known in the art of record to suppress mineralization in the periodontal ligament and to prevent the adhesion of teeth.

The specification does not provide guidance on any method of administration of full-length human RGD-CAP for suppression of mineralization and adhesion of the periodontal ligament at the time of tooth transplantation. The specification contemplates general approaches to the method of claim 4, however, no working examples are provided. Further, while the specification contemplates applying full-length human GD-CAP to the periodontal ligament or to the dental socket at the time of tooth transplantation; the specification does not specify what is meant by application. The term application includes topical application and subcutaneous injection, amongst others. The specification does not provide any working examples demonstrating that any route of application of full-length human GD-CAP can suppress mineralization and adhesion of the periodontal ligament by using full-length human RGD-CAP at the time of tooth transplantation. All of the working examples read on *in vitro* methods of using full-length human RGD-CAP for suppressing ALP activity and bone nodule formation. Further, an effective rout of administration of RGD-CAP in order to suppress mineralization and adhesion of the periodontal ligament at the time of tooth transplantation was not known in the art of record at the time of filing.

The specification does not describe the duration of the half-life or the stability of human RGD-CAP or its variants. Further, the specification does not enable any and all methods of administering full-length human RGD-CAP or its variants at the time of tooth transplantation, such as intravenous, topical, or sub dermal application. The specification contemplates that full length human RGD-CAP will be applied to the periodontal ligament or to the dental socket at the

time of tooth transplantation, however no dosage of full-length human GD-CAP is specified. The half-life of protein drugs such as tissue type plasmiongen activators (t-PA) can range from 4 minutes for wild-type t-PA to 20 min for a t-PA with a single amino acid substitution. {Verstraete M. (1999) Ann Acad Med Singapore. 28:424-33}. This indicates that proteins that differ by a single amino acid can have vastly different stabilities *in vitro*. There are no working examples that teach that a specific amount or range of amounts of full-length human RGD-CAP, or variants thereof, are effective at suppressing mineralization and adhesion of the periodontal ligament by using RGD-CAP at the time of tooth transplantation. Further, the ability of full-length or variants of human RGD-CAP to suppress mineralization and adhesion of the periodontal ligament at the time of tooth transplantation was not known in the art of record at the time of filing. Given the lack of guidance in the specification on the necessary functional domains and stability of non-human RGD-CAP proteins, and human RGD-CAP protein variants, the lack of teachings on how to make any agent containing full-length human RGD-CAP, the lack of teachings in the art on an agent containing full-length human RGD-CAP, the complete lack of teachings in the specification describing any method of administering full-length human RGD-CAP, and the lack of teachings in the art that full-length human RGD-CAP can be used during tooth transplantation to suppress mineralization and adhesion in the periodontal ligament, the skilled artisan would be unable to practice the invention as claimed without extensive and arduous experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 refers to a method of "using" RGD-CAP at the time of tooth transplantation. The term "using" is vague and indefinite. "Using" encompasses any rout of administering, such as intravenous, topical or intra-dermal. It is not clear from the body of the claim what "using" means, and therefore it is not an effective method step. The metes and bounds of claim 4 cannot be determined.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Skonier et al. {Skonier et al. (1992) DNA Cell Biol. 1992 Sep; 11:511-22}.

Skonier et al. teaches a cDNA clone that encodes βIG-H3 (RGD-CAP) (pg. 511, Abstract). Specifically, Skonier et al. teaches that the cDNA of βIG-H3 encodes a protein with "683 amino acids, which contained an amino-terminal secretory sequence and a carboxy-terminal Arg-Gly-Asp (RGD) sequence that can serve as a ligand recognition site for several integrins" (pg. 511, Abstract). Skonier et al. provides guidance on the use of COS cells to produce βIG-H3 after transfection with plasmids encoding the cDNA of βIG-H3 (pg. 511, Abstract). Further Skonier et al. teaches that "beta IG-H3 also contained short amino acid regions homologous to similar regions in Drosophila fasciclin-I and four homologous internal domains,

which can be folded into a potential bivalent structure and could act as a bridge between cells expressing the appropriate ligand" (pg. 511 Abstract). The βIG-H3 protein taught by Skonier et al. is encoded by NM_000358(SEQ ID NO:1), which also encodes the preferred RGD-CAP (SEQ ID NO:2) of the present invention (Specification, page 7, line 3, amended paragraph). Thus, by teaching all the structural limitations of the claims as written, Skonier et al. anticipates the instant invention as claimed.

Applicant should note that intended use is not given patentable weight in claims that define a structure with functional language that reads solely on intended use. "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or In re Best, 195 USPQ 430, 433 (CCPA 1997). It is noted that the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand-alone. The MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." In re Casey, 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02).

Claim 4 is free of the prior art of record

No claims allowed

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy J Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703)-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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